Joubert syndrome

Joubert syndrome is a disorder that affects many parts of the body. The signs and symptoms of this condition vary among affected individuals, even among members of the same family.

The hallmark feature of Joubert syndrome is a brain abnormality called the molar tooth sign, which can be seen on brain imaging studies such as magnetic resonance imaging (MRI). This sign results from the abnormal development of regions near the back of the brain called the cerebellar vermis and the brainstem. The molar tooth sign got its name because the characteristic brain abnormalities resemble the cross-section of a molar tooth when seen on an MRI.

Most infants with Joubert syndrome have weak muscle tone (hypotonia) in infancy, which evolves into difficulty coordinating movements (ataxia) in early childhood. Other characteristic features of the condition include episodes of unusually fast or slow breathing in infancy and abnormal eye movements. Most affected individuals have delayed development and intellectual disability, which range from mild to severe. Distinctive facial features are also characteristic of Joubert syndrome; these include a broad forehead, arched eyebrows, droopy eyelids (ptosis), widely spaced eyes, low-set ears, and a triangle-shaped mouth.

Joubert syndrome can include a broad range of additional signs and symptoms. The condition is sometimes associated with other eye abnormalities (such as retinal dystrophy, which can cause vision loss), kidney disease, liver disease, skeletal abnormalities (such as the presence of extra fingers and toes), and hormone (endocrine) problems. When the characteristic features of Joubert syndrome occur in combination with one or more of these additional signs and symptoms, researchers refer to the condition as "Joubert syndrome and related disorders (JSRD)."

Frequency

Joubert syndrome is estimated to affect between 1 in 80,000 and 1 in 100,000 newborns. However, this estimate may be too low because Joubert syndrome has such a large range of possible features and is likely underdiagnosed.

Genetic Changes

Joubert syndrome and related disorders can be caused by mutations in at least 10 genes. The proteins produced from these genes are known or suspected to play roles in cell structures called cilia. Cilia are microscopic, finger-like projections that stick out from the surface of cells and are involved in chemical signaling. Cilia are important for the structure and function of many types of cells, including brain cells (neurons)

and certain cells in the kidneys and liver. Cilia are also necessary for the perception of sensory input (such as sight, hearing, and smell).

Mutations in the genes associated with Joubert syndrome and related disorders lead to problems with the structure and function of cilia. Defects in these cell structures probably disrupt important chemical signaling pathways during development. Although researchers believe that defective cilia are responsible for most of the features of these disorders, it remains unclear how they lead to specific developmental abnormalities.

Mutations in the 10 genes known to be associated with Joubert syndrome and related disorders only account for about half of all cases of these conditions. In the remaining cases, the genetic cause is unknown.

Inheritance Pattern

Joubert syndrome typically has an autosomal recessive pattern of inheritance, which means both copies of a gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they usually do not show signs and symptoms of the condition.

Rare cases of Joubert syndrome are inherited in an X-linked recessive pattern. In these cases, the causative gene is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- agenesis of cerebellar vermis
- cerebello-oculo-renal syndrome
- cerebellooculorenal syndrome 1
- CORS
- familial aplasia of the vermis
- JBTS
- Joubert-Bolthauser syndrome

Diagnosis & Management

These resources address the diagnosis or management of Joubert syndrome:

- GeneReview: Joubert Syndrome and Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1325
- Genetic Testing Registry: Familial aplasia of the vermis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0431399/
- Genetic Testing Registry: Joubert syndrome 10
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2749019/
- Genetic Testing Registry: Joubert syndrome 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1842577/
- Genetic Testing Registry: Joubert syndrome 3
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1837713/
- Genetic Testing Registry: Joubert syndrome 4
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1846790/
- Genetic Testing Registry: Joubert syndrome 5
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1857780/
- Genetic Testing Registry: Joubert syndrome 6
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853153/
- Genetic Testing Registry: Joubert syndrome 7
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1969053/
- Genetic Testing Registry: Joubert syndrome 8
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2676771/
- Genetic Testing Registry: Joubert syndrome 9
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2676788/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Health Topic: Cerebellar Disorders
  https://medlineplus.gov/cerebellardisorders.html

Genetic and Rare Diseases Information Center

- Joubert syndrome
  https://rarediseases.info.nih.gov/diseases/6802/joubert-syndrome

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Joubert-Syndrome-Information-Page

Educational Resources

- Disease InfoSearch: Familial aplasia of the vermis
  http://www.diseaseinfosearch.org/Familial+aplasia+of+the+vermis/8373
- Joubert Syndrome & Related Disorders Foundation: Overview
  http://jsrdf.org/what-is-js/
- MalaCards: joubert syndrome and related disorders
  http://www.malacards.org/card/joubert_syndrome_and_related_disorders
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Joubert%20syndrome&type=profile
- Orphanet: Joubert syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=475

Patient Support and Advocacy Resources

- Ciliopathy Alliance (UK)
  http://www.ciliopathyalliance.org/
- Joubert Syndrome & Related Disorders Foundation
  http://jsrdf.org/

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/joubert-syndrome/
- University of Washington Joubert Research Program
  http://depts.washington.edu/joubert/joubertsyndrome.php

GeneReviews

- Joubert Syndrome and Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1325

Genetic Testing Registry

- Familial aplasia of the vermis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0431399/
- Joubert syndrome 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1842577/
- Joubert syndrome 3
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1837713/
- Joubert syndrome 4
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1846790/
- Joubert syndrome 5
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1857780/
- Joubert syndrome 6
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853153/
- Joubert syndrome 7
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1969053/
- Joubert syndrome 8
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2676771/
- Joubert syndrome 9
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2676788/
- Joubert syndrome 10
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2749019/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Joubert+syndrome%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28joubert+syndrome%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- JOUBERT SYNDROME 1
  http://omim.org/entry/213300
- JOUBERT SYNDROME 2
  http://omim.org/entry/608091
- JOUBERT SYNDROME 3
  http://omim.org/entry/608629
- JOUBERT SYNDROME 4
  http://omim.org/entry/609583
- JOUBERT SYNDROME 5
  http://omim.org/entry/610188
- JOUBERT SYNDROME 6
  http://omim.org/entry/610688
- JOUBERT SYNDROME 7
  http://omim.org/entry/611560
- JOUBERT SYNDROME 8
  http://omim.org/entry/612291
- JOUBERT SYNDROME 9
  http://omim.org/entry/612285
- JOUBERT SYNDROME 10
  http://omim.org/entry/300804

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